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(58) Field of search
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(54) Injectable solution containing
theophylline and a basic amino acid

(57) An injectable solution comprising
a basic amino acid and theophylline, for
use in the treatment of cardiac asthma
and allergic asthma. The basic amino
acid is especially lysine. Also disclosed
is a compound formed by reaction of
lysine and theophylline.

GB 2 094 142

SPECIFICATION

Injectable solution containing theophylline

5 The present invention relates to injectable solutions. It is well known that a mixture of theophylline and ethylenediamine (known as aminophylline) is used in the treatment of bronchial spasm and relaxes involuntary muscle. Aminophylline can be adminis-
 10 tered by intravenous injection in which case a sterile solution with a pH of from 9.2 to 9.6 is normally employed. Aminophylline can also have unpleasant side effects such as nausea, vomiting, hyperventilation and palpitations.

15 Theophylline has also been used for clinical purposes in combination with salts containing metal cations such as sodium. This can increase the solubility of theophylline in water but the presence of metal ions such as sodium is thought to be
 20 undesirable.

The present invention provides an injectable solution comprising a basic amino acid, for example lysine or arginine and theophylline.

A preferred amino acid is lysine although any
 25 naturally occurring basic amino acid, preferably one which occurs naturally in the human body and is thus readily metabolised may be suitable. The present invention will be illustrated in more detail with reference to the following Example.

Example

Our studies have indicated that when lysine and theophylline are combined in solution, a novel complex is formed, which will be referred to herein
 35 as Lysinium Theophyllinate. The presence of a complex of some kind has been indicated by ultraviolet spectroscopy, and it should be understood that the invention includes within its scope this novel compound *per se* as well as a solution thereof, for
 40 example an aqueous solution.

Our investigations indicate that such an aqueous solution containing theophylline in combination with lysine has significant advantages when used for
 45 injections in the treatment of complaints such as allergic asthma and cardiac asthma as compared with the conventional aminophylline.

These advantages include the absence of the toxic ethylenediamine molecule, and the fact that solutions having a pH which approaches more closely
 50 that of the blood can readily be prepared. It is also believed that the solution of the present invention is more readily utilised in the bloodstream.

The molar ratio of lysine to theophylline in the injectable solution is preferably approximately
 55 0.75:1.

The following is an Example of the preparation of an injectable solution according to the invention.

Example

be terminally sterilised by autoclaving. Ultraviolet spectroscopy indicated the presence in the solution of a complex, Lysinium Theophyllinate. The solution provided a readily assimilable injectable solution
 70 including theophylline and not having the toxic effects attributable to ethylenediamine.

It is envisaged that the novel complex may be utilised for topical application, for example as a nasal spray for the treatment of asthma and as a
 75 rectal suppository for the same treatment.

CLAIMS

1. An injectable solution comprising a basic
 80 amino acid and theophylline.
2. A solution as claimed in claim 1 wherein the amino acid is lysine.
3. A solution as claimed in claim 1 or claim 2 wherein the molar ratio of lysine to theophylline is
 85 approximately 0.75:1.
4. The use of a solution as claimed in any of the preceding claims in the treatment of cardiac asthma and allergic asthma.
5. A compound formed by the reaction of lysine
 90 and theophylline.
6. A process for preparing a compound as claimed in claim 5 which comprises reacting lysine with theophylline.
7. A solution as claimed in claim 1 substantially
 95 as hereinbefore described in the Example.

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